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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/408,025	09/29/99	NARANG H	0769.00125

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EXAMINER	
ZEMAN, R	

ART UNIT	PAPER NUMBER
1645	3

DATE MAILED: 01/24/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/408,023	Narang
Examiner	**Group Art Unit**
Robert A. Zeman	1645

☒ Responsive to communication(s) filed on *Sep 29, 1999*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-43* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-43* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Oath/Declaration

Applicant is requested to clarify the status of this case with respect to the priority document PCT/GB98/00374. The first sentence of the specification states that the present application is a continuation-in-part of PCT/GB98/00374. It is noted that the title of that document is "DIAGNOSIS OF NEURO-DEGENERATIVE DISORDERS".

The oath refers to the invention entitled "**Monitoring of Liquids for Disease-Associated Materials".**

Thus it is unclear to what specification the oath in fact refers.

If this application is a continuation-in-part, then the oath or declaration is defective. . A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not state that the person making the oath or declaration in a continuation-in-part application filed under the conditions specified in 35 U.S.C. 120 which discloses and claims subject matter in addition to that disclosed in the prior copending application, acknowledges the duty to disclose to the Office all information known to the person to be material to patentability as defined in 37 CFR 1.56 which occurred between the filing date of the prior application and the national or PCT international filing date of the continuation-in-part application.

Specification

– maintain withdrawn

The use of the trademarks Tween and Bio-Dot has been noted in this application. Each should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claims 1-43 as originally filed are pending and under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-14 recite methods and kits for monitoring liquids for the presence of disease-modified or associated proteins comprising of the steps concentrating the proteins by contacting a solid non-buoyant particulate material having free ionic valencies and subsequently monitoring the concentrated protein via a myriad of conventional assays including: ELISA, electron

microscopy, polymerase chain reaction (PCR) and Western blotting. While applicant recites the conventional assays in sufficient detail for one of skill in the art to perform them in general, Applicant fails to describe the claimed invention in sufficient detail to enable one of skill in the art to make and use said invention. The specification discloses that the disease-modified or associated proteins in a biological fluid (urine) are concentrated by the addition of granular calcium phosphate and a "suitable buffer". Only granular calcium phosphate was given as an example the solid non-buoyant particulate material,However, Applicant fails to describe what quantity or purity of calcium phosphate is required to practice the said invention and does not describe what exemplifies a "suitable buffer" or what volume and/or molarity is required for use in the claimed invention. Applicant does describe the use of "non-buoyant particulate flock" (see page 21) but provides no information on what it is, where it could be obtained, or how to make it. Consequently, it would require undue experimentation by one of skill in the art to make and use the claimed invention.

Claims 15-18 recite methods for concentrating disease-modified or associated proteins from a sample of liquid. In addition to the aforementioned deficiencies, these claims have an additional enablement issue. Step (k) of claim 15 recites "collecting supernatant containing the disease-modified or associated proteins" after centrifugation. This would not result in the recovery of proteins as claimed by the Applicant. Applicant discloses that the proteins are bound by the particulate matter and that the buffers are used to "remove" any unbound material.

Collecting this "wash buffer" would not result in recovery of proteins, as claimed, but only in the recovery of buffer.

Claims 19-30 recite methods of monitoring a liquid for the presence of disease-modified or associated proteins, protein fragments, viruses and virus fragments utilizing a solid filter medium having free ionic valencies. Claims 22-24 further recite that said filter medium comprises a sheet of either gauze fiber material or cotton fiber material having a pore size of 1-100 microns. However applicant fails to describe either the source of said filter material nor the means for its manufacture. Insofar as can be determined, the art does not teach the existence of a fiber sheet (of either cotton or gauze) with a weave interval of 1 to 100 microns. Hence, it would require undue experimentation by one of skill in the art to make and/or use the claimed invention as described.

Claims 31-43 recite methods of monitoring a liquid for the presence of disease-modified or associated proteins, protein fragments, viruses and virus fragments utilizing a solid, non-buoyant particulate matter having free ionic valencies (granular calcium phosphate) **and** a solid filter medium having free ionic valencies. Applicant further recites that said filter medium comprises a sheet of either gauze fiber material or cotton fiber material having a pore size of 1-100 microns. Combining the use of the particulate matter and the solid filter media into a single method would not allow one of skill in the art to make and use the claimed invention since the manufacture and use of each of the aforementioned components are not enabled, as discussed above.

Claims 3, 13, 17, 21 and 33 specifically recite the use of the aforementioned inventions to monitor urine for the presence of disease-modified or associated proteins, protein fragments, viruses, or virus fragments. Applicant, however fails to describe what particular proteins or viruses would be present in the urine; or what specific reagents (i.e. antibodies etc.) would be needed to detect said proteins and viruses or how to associate them with particular diseases. Insofar as can be determined, the art does not teach the presence of disease-modified or associated proteins or viruses in urine to be associated with the diseases as claimed by applicant. Hence, it would require undue experimentation by one of skill in the art to make and/or use the claimed invention as described.

Claim 9 recites the amplification of concentrated proteins by PCR and subsequent monitoring by a restriction length method. The aforementioned methods require nucleic acids not protein for their practice. The specification does not teach how to perform PCR using proteins and hence is not enabled.

Claim 10 recites use of concentrated proteins in a hybridization reaction and subsequently monitored using Western blotting. The specification does not describe what "hybridization reaction" is to be used or how to perform said reaction and hence the claim is not enabled

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4, 11, 14, 15, 18, 22, 23, 31 and 34-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 11, 15, and 31 recite the term "solid, non-buoyant particulate material having free ionic valencies" which is vague and indefinite. It is unclear whether "solid" includes or excludes porous materials. Does "non-buoyant" apply to the solid when it is in just water or all liquids? What type of free valencies are being referred to? Positive charges? Negative charges? A combination? Use of these terms makes it impossible to determine the metes and bounds of the claimed inventions.

Claims 4, 14, 18 and 34 recite the term "calcium phosphate in granular form" which is vague and indefinite. It is unclear whether the calcium phosphate needs to be pure or not and hence it is impossible to determine the metes and bounds of the claimed inventions.

Claims 22 and 35 recite the term "comprises a gauze fiber material" which is vague and indefinite. It is unclear what the exact composition of said material is and hence it is impossible to determine the metes and bounds of the claimed invention.

Claims 23 and 36 recite the term "comprises a cotton fiber material" which is vague and indefinite which is vague and indefinite. It is unclear what the exact composition of said material is and hence it is impossible to determine the metes and bounds of the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-21, 24-33 and 37-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schenk et al. (U.S. Patent 5,593,846), in view of Alaska et al. (U.S. Patent 5,744,587) and Chu et al. (U.S. Patent 4,604,208).

Claims 1-10 and 15-18 recite methods for monitoring/concentrating liquids for the presence of disease-modified or associated proteins comprising concentrating the said proteins by contacting a solid non-buoyant particulate material having free ionic valencies and subsequently monitoring the said concentrated protein via a myriad of conventional assays including: ELISA, electron microscopy, polymerase chain reaction (PCR) and Western blotting. Schenk et al. disclose the monitoring of Alzheimer's disease-associated protein, beta-amyloid protein (βAP), in biological fluids as means of predicting Alzheimer's disease. Schenk et al. further disclose that βAP is present in very low concentrations in biological fluids (see abstract) such as blood, cerebrospinal fluid (CSF), urine, or peritoneal fluid (see column 4 lines 39-42). Schenk et al. also disclose methods for monitoring the βAP levels in said biological fluids which include Western blotting and ELISA. While the disclosed ELISA is capable of detecting the Alzheimer's disease-associated protein at extremely low concentrations, it is disclosed by Schenk et al. that the βAP

must be concentrated for use in Western blotting and assays with similar sensitivity. While Schenk et al., disclose the use of affinity purification to concentrate βAP, they do not disclose the use of solid, non-buoyant particulate matter having free ionic valencies (granular calcium phosphate) or a solid filter medium having free ionic valencies. Alaska et al. disclose the use of hydroxyapatite, which is a solid, non-buoyant particulate material, for the binding of proteins in biological fluids, but not the use of granular calcium phosphate for the same purpose. However, as Applicant discloses on page 7 of the specification, granular calcium phosphate and hydroxyapatite are similar compounds. Both are solid, non-buoyant particulate materials with free ionic valences. Applicant further discloses that hydroxyapatite has been previously used to "purify and concentrate viruses and their related soluble antigens" (see page 7-8). Consequently, it would have been obvious to one of skill in the art to use "like" compounds in order to optimize the system. One would have a high expectation of success since, as applicant points out, hydroxyapatite and granular calcium phosphate are similar compound. Similarly, it would have been obvious to one of skill in the art to use the concentration methods disclosed by Alaska et al. in the monitoring methods disclosed by Schenk et al, because their combination would yield a higher concentration of the Alzheimer's disease-associated βAP which could then be used in more cost effective detection assays.

Claims 19-21 and 24-30 recite a methods for monitoring a liquid for the presence of biological material comprising the use of a solid filter medium having free ionic valencies and subsequently testing bound material by electron microscopy, ELISA, or Western blotting. Chu et

al. disclose that the use of microporous membranes for the removal/concentration of proteins and microorganisms is well known in the art (see columns 1 -2). Additionally, Chu et al disclose the use of anionic microporous membrane (i.e. a solid filter medium with free ionic valencies) for the purification of liquids. While Chu et al. disclose the use of microporous membranes for protein/virus concentration , they do not disclose the use said membranes for the concentration for monitoring disease associated proteins. Therefore, it would have been obvious to one of skill in the art to use the concentration methods disclosed by Chu et al. with the monitoring methods disclosed by Schenk et al, because their combination would yield a higher concentration of the Alzheimer's disease-associated βAP which could then be used in more cost effective detection assays.

Claims 31-34 and 37-43 recite methods of monitoring a liquid for the presence of disease-modified or associated proteins, a protein fragments, viruses and virus fragments utilizing a solid, non-buoyant particulate matter having free ionic valencies (granular calcium phosphate) **and** a solid filter medium having free ionic valencies. Applicant further recites that said filter medium comprises a sheet of either gauze fiber material or cotton fiber material having a pore size of 1-100 microns. As stated above, Alaska et al disclose the use of hydroxyapatite and Chu et al. disclose the use of a anionic microporous membrane for the binding of proteins and/or microorganisms in a biological fluid. Additionally, Alaska et al discloses that it is advantageous to combine the use of hydroxyapatite with other purification and concentration techniques including ultrafiltration (see Column 3, lines 57-61). Consequently, it would have been obvious

for one of skill in the art to combine the use of solid, non-buoyant particulate matter having free ionic valencies (optimized for the use of granular calcium phosphate) and the anionic microporous membrane of Chu et al. with the monitoring methods of Schenk et al. One would expect said the combining of the concentration methods of Chu et al. and Alaska et al. to increase efficiency since such a combination was encouraged by Alaska et al. Combination of the concentration methods of Chu et al. and Alaska et al. with the monitoring methods of Schenk et al. would result in the need for smaller samples to be obtained from patients and the ability to use more cost effective detection assays.

Claims 11-14 recite an ELISA kit and a solid, non-buoyant particulate material (granular calcium phosphate) added for binding the proteins to be tested. For the reasons described above, the use of granular calcium would have been obvious in light of the prior art. Additionally, bundling a materials to used together in the form of a kit also would have been obvious to one of skill in the art for it would result in greater ease of use and would be more economical.

Conclusion

No claim is allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (703) 308-7991. The examiner can be reached between the hours of 7:30 am and 4:00 pm Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, Donna Wortman, Primary Examiner can be reached at (703) 308-1032 or the examiner's supervisor, Anthony Caputa, can be reached at (703)308-3995.

DONNA WORTMAN
PRIMARY EXAMINER

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1/12/2000